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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 09   CA/CAplus records now contain indexing from 1907 to the
                   present
 NEWS  4  AUG 05   New pricing for EUROPATFULL and PCTFULL effective
                   August 1, 2003
 NEWS  5  AUG 13   Field Availability (/FA) field enhanced in BEILSTEIN
 NEWS  6  AUG 18   Data available for download as a PDF in RDISCLOSURE
 NEWS  7  AUG 18   Simultaneous left and right truncation added to PASCAL
 NEWS  8  AUG 18   FROSTI and KOSMET enhanced with Simultaneous Left and Righ
                   Truncation
 NEWS  9  AUG 18   Simultaneous left and right truncation added to ANABSTR
 NEWS 10  SEP 22   DIPPR file reloaded
 NEWS 11  SEP 25   INPADOC: Legal Status data to be reloaded
 NEWS 12  SEP 29   DISSABS now available on STN
 NEWS 13  OCT 10   PCTFULL: Two new display fields added
 NEWS 14  OCT 21   BIOSIS file reloaded and enhanced
 NEWS 15  OCT 28   BIOSIS file segment of TOXCENTER reloaded and enhanced

 NEWS EXPRESS  OCTOBER 01 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
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FILE 'HOME' ENTERED AT 19:09:17 ON 30 OCT 2003

=> index bioscience medicine
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.63       0.63

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
      BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
      CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS, DDFB, DDFU,
      DGENE, DRUGB, DRUGLAUNCH, ...' ENTERED AT 19:10:57 ON 30 OCT 2003
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71 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

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=> s tag? (s)(vecto? or plasmi?) (s) cleav? (s) secret?
          4   FILE AGRICOLA
          1   FILE BIOBUSINESS
        237   FILE BIOTECHABS
        237   FILE BIOTECHDS
         26   FILE BIOTECHNO
          4   FILE CABA
          8   FILE CANCERLIT
          2   FILE CAPLUS
          1   FILE CEABA-VTB
  19 FILES SEARCHED...
          1   FILE DISSABS
         38   FILE DGENE
  25 FILES SEARCHED...
          1   FILE DRUGU
         22   FILE EMBASE
         26   FILE ESBIOBASE
          4*  FILE FEDRIP
          1   FILE FSTA
         10   FILE GENBANK
  40 FILES SEARCHED...
         34   FILE IFIPAT
         13   FILE LIFESCI
          7   FILE PASCAL
          1   FILE PROMT
         27   FILE SCISEARCH
        152   FILE USPATFULL
  63 FILES SEARCHED...
          2   FILE USPAT2
         15   FILE WPIDS
         15   FILE WPINDEX
          1   FILE NLDB

  27 FILES HAVE ONE OR MORE ANSWERS,   71 FILES SEARCHED IN STNINDEX

L1   QUE TAG? (S)(VECTO? OR PLASMI?) (S) CLEAV? (S) SECRET?

=> d rankn
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Answer set was created in a file.  Enter DISPLAY HISTORY to see where
the answer set was created.  Use the File command to change to that
file, then display the answer.

=> d rank
F1          237   BIOTECHABS
F2          237   BIOTECHDS
F3          152   USPATFULL
F4           38   DGENE
F5           34   IFIPAT
F6           27   SCISEARCH
F7           26   BIOTECHNO
F8           26   ESBIOBASE
F9           22   EMBASE
F10          15   WPIDS
F11          15   WPINDEX
F12          13   LIFESCI
F13          10   GENBANK
F14           8   CANCERLIT
F15           7   PASCAL
F16           4   AGRICOLA
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F17           4    CABA
F18           4*   FEDRIP
F19           2    CAPLUS
F20           2    USPAT2
F21           1    BIOBUSINESS
F22           1    CEABA-VTB
F23           1    DISSABS
F24           1    DRUGU
F25           1    FSTA
F26           1    PROMT
F27           1    NLDB


=> file f1-f10
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       2.75       3.38

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FILE 'BIOTECHDS' ENTERED AT 19:13:47 ON 30 OCT 2003
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   7 FILES SEARCHED...
L2          577 TAG? (S)(VECTO? OR PLASMI?) (S) CLEAV? (S) SECRET?

=> dup rem
ENTER L# LIST OR (END):l2
DUPLICATE IS NOT AVAILABLE IN 'DGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L2
L3           488 DUP REM L2 (89 DUPLICATES REMOVED)

<------User Break------>

SEARCH ENDED BY USER

=> s l3 (s) histidin?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L26 (S) HISTIDIN?'
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PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L28 (S) HISTIDIN?'
L4          62 L3 (S) HISTIDIN?

=> s l4 and enterokin?
L5          23 L4 AND ENTEROKIN?

=> s l5 and trypsi?
L6          12 L5 AND TRYPSI?

=> s l6 and (neuros? or kallikr?)
L7          10 L6 AND (NEUROS? OR KALLIKR?)

=> d ti l7 1-10

L7   ANSWER 1 OF 10  USPATFULL on STN
TI     Novel human G-protein coupled receptor, HGPRBMY34, and variants and
       methods of use thereof

L7   ANSWER 2 OF 10  USPATFULL on STN
TI     DNA encoding the human serine protease EOS

L7   ANSWER 3 OF 10  USPATFULL on STN
TI     DNA encoding the human serine protease T

L7   ANSWER 4 OF 10  USPATFULL on STN
TI     DNA encoding the human serine protease C-E

L7   ANSWER 5 OF 10  USPATFULL on STN
TI     DNA encoding the human serine protease T

L7   ANSWER 6 OF 10  USPATFULL on STN
TI     DNA encoding the human serine protease EOS

L7   ANSWER 7 OF 10  USPATFULL on STN
TI     DNA encoding the human serine protease EOS

L7   ANSWER 8 OF 10  USPATFULL on STN
TI     DNA encoding the human serine protease T

L7   ANSWER 9 OF 10  USPATFULL on STN
TI     DNA encoding the human serine protease EOS

L7   ANSWER 10 OF 10  USPATFULL on STN
TI     DNA


=> d ibib abs l7 1-10

L7   ANSWER 1 OF 10  USPATFULL on STN
ACCESSION NUMBER:       2003:219687  USPATFULL
TITLE:                  Novel human G-protein coupled receptor, HGPRBMY34, and
                        variants and methods of use thereof
INVENTOR(S):            Ramanathan, Chandra S., Wallingford, CT, UNITED STATES
                        Gopal, Shuba, New York, NY, UNITED STATES
                        Mintier, Gabriel A., Hightstown, NJ, UNITED STATES
                        Feder, John N., Belle Mead, NJ, UNITED STATES

                             NUMBER        KIND    DATE
                        ---------------- ------ --------
PATENT INFORMATION:     US 2003152977      A1   20030814
APPLICATION INFO.:      US 2002-314076     A1   20021206  (10)

                               NUMBER        DATE
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PRIORITY INFORMATION: US 2001-338371P 20011206 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 8649
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes the novel human G-protein coupled receptor (GPCR) HGPRBMY34 and its encoding polynucleotide. Also described are expression vectors, host cells, antisense molecules, and antibodies associated with the HGPRBMY34 polynucleotide and/or polypeptide of this invention. In addition, methods for treating, diagnosing, preventing, and screening for disorders or diseases associated with abnormal biological activity of HGPRBMY34 are described, as are methods for screening for modulators, e.g., agonists or antagonists, of HGPRBMY34 activity and/or function.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 2 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:310801 USPATFULL
TITLE: DNA encoding the human serine protease EOS
INVENTOR(S): Darrow, Andrew, Lansdale, PA, United States
Qi, Jenson, Branchburg, NJ, United States
Andrade-Gordon, Patricia, Doylestown, PA, United States
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6485957	B1	20021126
APPLICATION INFO.:	US 1999-387375		19990831 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-303162, filed on 30 Apr 1999
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Achutamurthy, Ponnathapu
ASSISTANT EXAMINER: Moore, William W.
LEGAL REPRESENTATIVE: Wallen, III, John W.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 2185
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease EOS. The deduced amino acid sequence, and it alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease EOS mRNA is expressed in platelets and leukocytes and more specifically eosinophils. Although this protease is abundantly expressed in ovary, retina and stomach, where it may perform important functions, its expression in platelets and certain cells of the immune system suggests that it may play roles in thrombosis and in the immune process. Enzymatically active protease EOS is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 3 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:301210 USPATFULL
TITLE: DNA encoding the human serine protease T

INVENTOR(S): Darrow, Andrew, Lansdale, PA, UNITED STATES
Qi, Jenson, Branchburg, NJ, UNITED STATES
Andrade-Grodon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002168754	A1	20021114
APPLICATION INFO.:	US 2002-41006	A1	20020107 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-386653, filed on 31 Aug 1999, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2046
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease T. The deduced amino acid sequence encodes a prepro form of 290 amino acids, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease T mRNA is expressed in stomach, testis, retina, fibroblasts, spinal cord, and several regions of the brain. Protease T mRNA is also found in leukocytes and in the Jurkat (ATCC TIB-152) T cell line. Thus, this protease is potentially involved in gastric, testicular, retinal, dematological, neurological/neurodegenerative and/or immunological disorders. The protease T gene maps to human chromosome 16p13.3 which is near the tryptase locus. Enzymatically active protease T, we have generated, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:294724 USPATFULL
TITLE: DNA encoding the human serine protease C-E
INVENTOR(S): Darrow, Andrew, Lansdale, PA, UNITED STATES
Qi, Jenson, Branchburg, NJ, UNITED STATES
Andrade-Grodon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002164767	A1	20021107
APPLICATION INFO.:	US 2002-40803	A1	20020107 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-386629, filed on 31 Aug 1999, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 2065
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease C-E. The deduced amino acid sequence, and it alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease C-E mRNA is expressed in pancreas, placenta, prostate, small intestine, stomach, spleen, fibroblasts and epidermis, as well as in certain regions of the brain

i.e., cerebellum, cerebral cortex, pituitary and hippocampus. Enzymatically active protease C-E, as produced using the methodologies described herein, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 5 OF 10 USPATFULL on STN

ACCESSION NUMBER:	2002:265929 USPATFULL
TITLE:	DNA encoding the human serine protease T
INVENTOR(S):	Darrow, Andrew, Lansdale, PA, UNITED STATES Qi, Jenson, Branchburg, NJ, UNITED STATES Andrade-Grodon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002146805	A1	20021010
APPLICATION INFO.:	US 2002-40655	A1	20020107 (10)

RELATED APPLN. INFO.:	Division of Ser. No. US 1999-386653, filed on 31 Aug 1999, PENDING
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003
NUMBER OF CLAIMS:	27
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	6 Drawing Page(s)
LINE COUNT:	2049

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease T. The deduced amino acid sequence encodes a prepro form of 290 amino acids, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease T mRNA is expressed in stomach, testis, retina, fibroblasts, spinal cord, and several regions of the brain. Protease T mRNA is also found in leukocytes and in the Jurkat (ATCC TIB-152) T cell line. Thus, this protease is potentially involved in gastric, testicular, retinal, dematological, neurological/neurodegenerative and/or immunological disorders. The protease T gene maps to human chromosome 16p13.3 which is near the tryptase locus. Enzymatically active protease T, we have generated, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 10 USPATFULL on STN

ACCESSION NUMBER:	2002:258877 USPATFULL
TITLE:	DNA encoding the human serine protease EOS
INVENTOR(S):	Darrow, Andrew, Lansdale, PA, UNITED STATES Qi, Jenson, Branchburg, NJ, UNITED STATES Andrade-Gordon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002142447	A1	20021003
APPLICATION INFO.:	US 2002-42091	A1	20020108 (10)

RELATED APPLN. INFO.:	Division of Ser. No. US 1999-387375, filed on 31 Aug 1999, PENDING
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003
NUMBER OF CLAIMS:	27
EXEMPLARY CLAIM:	1

NUMBER OF DRAWINGS: 17 Drawing Page(s)
LINE COUNT: 2153
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease EOS. The deduced amino acid sequence, and it alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease EOS mRNA is expressed in platelets and leukocytes and more specifically eosinophils. Although this protease is abundantly expressed in ovary, retina and stomach, where it may perform important functions, its expression in platelets and certain cells of the immune system suggests that it may play roles in thrombosis and in the immune process. Enzymatically active protease EOS is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:258876 USPATFULL
TITLE: DNA encoding the human serine protease EOS
INVENTOR(S): Darrow, Andrew, Lansdale, PA, UNITED STATES
Qi, Jenson, Branchburg, NJ, UNITED STATES
Andrade-Gordon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002142446	A1	20021003
APPLICATION INFO.:	US 2002-41264	A1	20020108 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-387375, filed on 31 Aug 1999, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Page(s)
LINE COUNT: 2167
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease EOS. The deduced amino acid sequence, and it alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease EOS mRNA is expressed in platelets and leukocytes and more specifically eosinophils. Although this protease is abundantly expressed in ovary, retina and stomach, where it may perform important functions, its expression in platelets and certain cells of the immune system suggests that it may play roles in thrombosis and in the immune process. Enzymatically active protease EOS is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 8 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:254200 USPATFULL
TITLE: DNA encoding the human serine protease T
INVENTOR(S): Darrow, Andrew, Lansdale, PA, United States
Qi, Jenson, Branchburg, NJ, United States
Andrade-Grodon, Patricia, Doylestown, PA, United States
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6458564	B1	20021001	
APPLICATION INFO.:	US 1999-386653		19990831	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Achutamurthy, Ponnathapu
ASSISTANT EXAMINER: Moore, William W.
LEGAL REPRESENTATIVE: Wallen, III, John W.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 2073
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease T. The deduced amino acid sequence encodes a prepro form of 290 amino acids, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease T mRNA is expressed in stomach, testis, retina, fibroblasts, spinal cord, and several regions of the brain. Protease T MRNA is also found in leukocytes and in the Jurkat (ATCC TIB-152) T cell line. Thus, this protease is potentially involved in gastric, testicular, retinal, dematological, neurological/neurodegenerative and/or immunological disorders. The protease T gene maps to human chromosome 16p13.3 which is near the tryptase locus. Enzymatically active protease T, we have generated, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 9 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:206201 USPATFULL
TITLE: DNA encoding the human serine protease EOS
INVENTOR(S): Darrow, Andrew, Lansdale, PA, UNITED STATES
Qi, Jenson, Branchburg, NJ, UNITED STATES
Andrade-Gordon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002110895	A1	20020815	
APPLICATION INFO.:	US 2002-41400	A1	20020108	(10)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-387375, filed on 31 Aug 1999, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Page(s)
LINE COUNT: 2166
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease EOS. The deduced amino acid sequence, and it alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease EOS mRNA is expressed in platelets and leukocytes and more specifically eosinophils. Although this protease is abundantly expressed in ovary, retina and stomach, where it may perform important functions, its expression in platelets and certain cells of the immune system suggests that it may play roles in thrombosis and in the immune process. Enzymatically active protease EOS is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 10 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:188232 USPATFULL
TITLE: DNA
INVENTOR(S): Darrow, Andrew, Lansdale, PA, United States
Qi, Jenson, Branchburg, NJ, United States
Andrade-Grodon, Patricia, Doylestown, PA, United States
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6426199	B1	20020730	
APPLICATION INFO.:	US 1999-386629		19990831	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Achutamurthy, Ponnathapu
ASSISTANT EXAMINER: Moore, William W.
LEGAL REPRESENTATIVE: Wallen III, John W.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 2090
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease C-E. The deduced amino acid sequence, and it alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease C-E mRNA is expressed in pancreas, placenta, prostate, small intestine, stomach, spleen, fibroblasts and epidermis, as well as in certain regions of the brain i.e., cerebellum, cerebral cortex, pituitary and hippocampus. Enzymatically active protease C-E, as produced using the methodologies described herein, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic l7 1-10

L7 ANSWER 1 OF 10 USPATFULL on STN
DETD [0187] Host cells transformed with **vectors** containing nucleotide sequences encoding a HGPRBMY34 protein, or fragments thereof, may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be **secreted** or contained intracellularly depending on the sequence and/or the **vector** used. As will be understood by those having skill in the art, expression **vectors** containing polynucleotides which encode a HGPRBMY34 protein can be designed to contain signal sequences which direct **secretion** of the HGPRBMY34 protein through a prokaryotic or eukaryotic cell membrane. Other constructions can be used to join nucleic acid. . . facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as **histidine**-tryptophan modules that allow purification on immobilized metals; protein A domains that allow purification on immobilized immunoglobulin; and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of **cleavable** linker sequences such as those specific for Factor XA or **enterokinase** (Invitrogen, San Diego, Calif.) between the purification domain and the HGPRBMY34 protein may be used to facilitate purification. One such expression **vector** provides for expression of a fusion protein containing HGPRBMY34 and a

nucleic acid encoding 6 **histidine** residues preceding a thioredoxin or an **enterokinase cleavage** site. The **histidine** residues facilitate purification on IMAC (immobilized metal ion affinity chromatography) as described by J. Porath et al., 1992, Prot. Exp. Purif., 3:263-281, while the **enterokinase cleavage** site provides a means for purifying the 6 **histidine** residue **tag** from the fusion protein. For a discussion of suitable **vectors** for fusion protein production, see D. J. Kroll et al., 1993; DNA Cell Biol., 12:441-453.

DETD . . . herein or otherwise known in the art, such as, for example, the method set forth in Arakawa et al. (J. **Neurosci**. 10:3507-3515 (1990)); increased sprouting of neurons may be detected by methods known in the art, such as, for example, the methods set forth in Pestronk et al. (Exp. Neurol. 70:65-82 (1980)) or Brown et al. (Ann. Rev. **Neurosci**. 4:17-42 (1981)); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody binding, Northern blot assay, etc.,. . .

DETD . . . Examples of such immunogenic proteins include, but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean **trypsin** inhibitor. Various adjuvants may be used to increase the immunological response, depending on the host species, including but not limited. . .

DETD . . . (1983); see also Levy et al., Science 228:190 (1985); During et al., Ann. Neurol. 25:351 (1989); Howard et al., J. **Neurosurg**. 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e.,. . .

DETD . . . G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are **trypsinized** and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are **trypsinized** and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM,. . .

L7 ANSWER 2 OF 10 USPATFULL on STN

SUMM Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification. . .

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding the hemagglutinin (HA) epitope and 6 **histidine** (6XHIS) codons for detection with the anti-HA antibody MoAb 12 CA5 (Boehringer Mannheim Corp., Indianapolis, Ind.) and affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBacl transplacement **plasmid** to generate PFEK-HA6XHIS-**TAG** FB.

DETD . . . 15 mM imidazole], followed by with a 1.5 ml wash with ds

H.sub.2O. Zymogen cleavage was carried out by adding **enterokinase** (10 U per 50 g of zymogen) (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 3 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification. . .

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6XHIS) codons for affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the 6XHIS affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified Drosophila expression **plasmid** to generate PFEK-6XHIS-**TAG64**.

DETD . . . Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole,), followed by with a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA beads in a 150 ul volume at. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0163] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0178] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997).

Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . Z. -m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . Ogawa, h., Takagi, K. -i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 4 OF 10 USPATFULL on STN

SUMM [0001] The members of the **trypsin**/chymotrypsin-like (S1) serine protease family are gaining recognition due to the increased awareness that these enzymes play pivotal roles in a multitude of diverse physiological processes. In addition to the classical functions the proteases **trypsin** and chymotrypsin perform during the digestive process, serine proteases also participate in regulating key amplification cascades through the proteolytic activation. . .

DETD . . .. and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . (Miller et al. (1990). J. Clin. Invest. 86:864-700), Chymotrypsinogen SW:P17538 (Tomita et al. (1989). Biochem. Biophys. Res. Commun. 158:569-75), Glandular **Kallikrein** 1 SW:P06870 (Fukushima et al. (1985). Biochemistry 24:8037-43), **Trypsinogen** I SW:P07477 (Emi et al. (1986). Gene 41:305-10) and the translated rat BSP2 partial sequence GB:AJ005642 (Davies, et al. (1998).. . .

DETD . . . in a manner similar to that previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6XHIS) codons for affinity purification on nickel resins. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBac 1 transplacement **plasmid** to generate PFEK-6XHIS-**TAG** FB.

DETD . . . mM Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole], followed by a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the Ni-NTA agarose bead-bound PFEK-protease C-E-6XHIS zymogen in a 150. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0167] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0182] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen

Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD [0189] Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-likeprotease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 5 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification. . .

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6.times.HIS) codons for affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the 6.times.HIS affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified Drosophila expression **plasmid** to generate PFEK-6.times.HIS-**TAG64**.

DETD . . . Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole,), followed by with a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA beads in a 150 ul volume at. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0165] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0180] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 6 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification. . .

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG. The term "pro-sequence" as used herein refers to a nucleotide sequence that encodes a cleavage site for a. . .

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding the hemagglutinin (HA) epitope and 6 **histidine** (6XHIS) codons for detection with the anti-HA antibody MoAb 12 CA5 (Boehringer Mannheim Corp., Indianapolis, Ind.) and affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBacl transplacement **plasmid** to generate PFEK-HA6XHIS-**TAG** FB. The purified **plasmid** DNA of the full length protease EOS cDNA was used as a template in a 100 .quadrature.l preparative PCR reaction. . .

DETD . . . 15 mM imidazole], followed by with a 1.5 ml wash with ds H.sub.2O. Zymogen cleavage was carried out by adding **enterokinase** (10 U per 50 .quadrature.g of zymogen) (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0129] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0152] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 7 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse

physiological processes, including digestive processes and regulatory amplification. . .

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding the hemagglutinin (HA) epitope and 6 **histidine** (6XHIS) codons for detection with the anti-HA antibody MoAb 12 CA5 (Boehringer Mannheim Corp., Indianapolis, Ind.) and affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBacl transplacement **plasmid** to generate PFEK-HA6XHIS-**TAG** FB.

DETD . . . 15 mM imidazole], followed by with a 1.5 ml wash with ds H.sub.2O. Zymogen cleavage was carried out by adding **enterokinase** (10 U per 50 .quadrature.g of zymogen) (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0161] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned CDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0184] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 8 OF 10 USPATFULL on STN

SUMM Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification. . .

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and

either inactivate (Takayama et al. (1997). J Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6XHIS) codons for affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the 6XHIS affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified Drosophila expression **plasmid** to generate PFEK-6XHIS-**TAG64**.

DETD . . . Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole,), followed by with a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA beads in a 150 ul volume at. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler376, 681-4.

DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 9 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification. . .

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding the hemagglutinin (HA) epitope and 6 **histidine** (6XHIS) codons for detection with the anti-HA antibody MoAb 12 CA5 (Boehringer Mannheim

Corp., Indianapolis, Ind.) and affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBacl transplacement **plasmid** to generate PFEK-HA6XHIS-**TAG** FB.

DETD . . . 15 mM imidazole], followed by with a 1.5 ml wash with ds H.sub.2O. Zymogen cleavage was carried out by adding **enterokinase** (10 U per 50 .quadrature.g of zymogen) (Novagen, Inc., Madison, Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0166] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0189] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . Z. -m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . Ogawa, h., Takagi, K. -i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 10 OF 10 USPATFULL on STN

SUMM The members of the **trypsin**/chymotrypsin-like (S1) serine protease family are gaining recognition due to the increased awareness that these enzymes play pivotal roles in a multitude of diverse physiological processes. In addition to the classical functions the proteases **trypsin** and chymotrypsin perform during the digestive process, serine proteases also participate in regulating key amplification cascades through the proteolytic activation. . .

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . (Miller et al. (1990). J. Clin. Invest. 86:864-700), Chymotrypsinogen SW:P17538 (Tomita et al. (1989). Biochem. Biophys. Res. Commun. 158:569-75), Glandular **Kallikrein** 1 SW:P06870 (Fukushima et al. (1985). Biochemistry 24:8037-43), **Trypsinogen** I SW:P07477 (Emi et al. (1986). Gene 41:305-10) and the translated rat BSP2 partial sequence GB:AJ005642 (Davies, et al. (1998).. . .

DETD . . . in a manner similar to that previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6XHIS) codons for affinity purification on nickel resins. A unique Xba I restriction

enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBac1 transplacement **plasmid** to generate PFEK-6XHIS-**TAG** FB.

DETD . . . mM Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole], followed by a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the Ni-NTA agarose bead-bound PFEK-protease C-E-6XHIS zymogen in a 150. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 3 76, 681-4.

DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

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INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, ...' ENTERED AT 19:10:57 ON 30 OCT 2003

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26	FILE BIOTECHNO
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8	FILE CANCERLIT
2	FILE CAPLUS
1	FILE CEABA-VTB
1	FILE DISSABS
38	FILE DGENE
1	FILE DRUGU
22	FILE EMBASE
26	FILE ESBIOBASE
4*	FILE FEDRIP
1	FILE FSTA
10	FILE GENBANK
34	FILE IFIPAT
13	FILE LIFESCI

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               15   FILE WPINDEX
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L4             62 S L3 (S) HISTIDIN?
L5             23 S L4 AND ENTEROKIN?
L6             12 S L5 AND TRYPSI?
L7             10 S L6 AND (NEUROS? OR KALLIKR?)

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                    32.81      36.19

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